Original Article

Obstetric Medicine

Obstetric Medicine
2019, Vol. 12(1) 22–26

DOI: 10.1177/1753495X18784081
journals.sagepub.com/home/obm
SAGE

Pregnancy in women known to be living with a single kidney

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Abstract

There is a paucity of data on pregnancy outcome in women living with a single kidney from all causes. Current thinking is extrapolated from living kidney donors, a group biased by strict selection criteria. We present a cohort of 26 women with a solitary functioning kidney; 11 women had an acquired single kidney of whom only 1 was a living donor and 15 had a congenital single kidney. Median time living with a single kidney was 28 years. None booked with hypertension or proteinuria. Urinary tract infection complicated 50% of pregnancies. Worryingly, 35% developed pre-eclampsia, gestational proteinuria or gestational hypertension. We propose pre-conceptual counselling, education on how to protect their single kidney, pre eclampsia prophylaxis with low-dose aspirin and close monitoring for urinary tract infection, hypertension and proteinuria with lower thresholds for pharmaceutical management. We have devised a Patient Information leaflet – 'Living with a single kidney, pregnancy and beyond'.

Keywords

Pregnancy, single kidney, solitary kidney

Received 24 January 2018; accepted 29 May 2018

Background

With increasing use of carefully screened and selected healthy living kidney donors for renal transplant, several studies suggested good long-term health outcomes for the donors. However, more recent meta-analyses, with longer follow-up and better matched control groups, indicate a small increase in blood pressure (BP) and minor deterioration in renal function in the short term.[1,2] After extended follow-up, increased risk of end-stage renal disease, cardiovascular and all-cause mortality is evident.[3] In addition, early reports suggested that post-donation pregnancy outcomes were unaffected in carefully selected donors;[4–6] however, recent and larger reports have noted an increase in the incidence of pre-eclampsia.[7–9] While some of these registries have a number of limitations, and should be interpreted with caution because of confounders such as maternal age and inter-pregnancy intervals, it is now suggested that women considering kidney donation should be made aware of the possible impact on future pregnancies as well as future renal health.[9]

Importantly, an increased risk of pre-eclampsia has recently been noted in a large cohort of women with unilateral renal agenesis (URA).[10] URA affects around 1 in 2000 people and has complex aetiology. It commonly arises in embryonic life from failure of the ureteric bud from the mesonephric duct, the metanephric mesenchyme or both to form or join properly. However, it may also arise following spontaneous involution of a multicystic dysplastic kidney and one-third of those with URA have an abnormality in the contralateral kidney, most commonly vesicoureteric reflux.[11] Unless the diagnosis has been made antenatally or in early life, it may not be possible to differentiate from other aetiologies, and the term solitary functioning kidney is used to reflect a wide range of disease processes. In practice, when not associated with pelvic organ anomaly, this condition largely appears to be considered benign by the obstetric community.

Kidney Research UK now advises that those living with a single kidney from all causes have an increased lifetime likelihood of developing proteinuria, hypertension and renal impairment and should have an annual review of BP and urinalysis in primary care.[12] It was our impression that women living with a single kidney were not aware of these issues.

We have been caring for considerable numbers of women entering pregnancy with a single kidney due to a variety of reasons other than being a living donor. In light of emerging data that caution should be exercised in extrapolating outcomes from healthy living donors, we sought to establish pregnancy and renal outcome in this heterogeneous group. We also explored their understanding of living with a single kidney, and aimed to utilise the unique contact with healthcare professionals during antenatal care to provide a package of support and education regarding protection of their vulnerable single kidney and lifelong monitoring to optimize renal and cardiovascular health.

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We present the clinical management, pregnancy and birth outcomes for a consecutive group of women living with a single or solitary functioning kidney from a variety of aetiologies. In addition, we present a suggested management plan incorporating pre-conceptual counselling, pregnancy care and life-long health education.

Method

Using our prospective Obstetric Medicine clinic database, we identified a group of women known to be living with a single kidney, either congenital or acquired, at the time of antenatal pregnancy booking between April 2009 and April 2015. Data were collected prospectively in a clinic database at the time of first review, usually in the first trimester. Further details about pre-pregnancy health, aetiology of single kidney, prior obstetric history and prior counselling or renal follow-up were obtained prospectively from individual medical records, the electronic maternity database and pathology reporting software. Pregnancy outcomes were recorded retrospectively with the main outcome measures being development of pre-eclampsia (new onset hypertension, BP $\geq$140/90 mmHg on two consecutive readings, after 20 weeks' gestation associated with significant proteinuria (urine protein:creatinine ratio (uPCR) >30 mg/mmol)),[13] gestational hypertension (new onset hypertension after 20 weeks' gestation), gestational proteinuria (defined as uPCR >30 mg/mmol in absence of urinary tract infection (UTI)), infective renal complications (defined as a clinical diagnosis of pyelonephritis), change in serum creatinine, gestation at onset of labour, mode of delivery and birthweight.

Results

We identified 26 women living with a single kidney who booked for antenatal care during this period, representing approximately 0.1% of our antenatal booking population. This is a minimum estimate, as some women particularly those with primary URA may be unaware of having a solitary kidney. In addition, not all women with a single kidney would have been referred to the Obstetric Medicine service.

The baseline characteristics for these 26 women are outlined in Tables 1 (acquired single kidney) and 2 (congenital single kidney) together with a summary of maternal and neonatal outcomes. They are divided into two groups for descriptive distinction and not to serve as a means to compare. The aim of the study is to provide a review of this mixed group who are often considered as a whole for the purposes of antenatal management. None of the women had been given a diagnosis of chronic kidney disease (CKD), met criteria for CKD as per NICE[14] or had ongoing urological or renal follow-up prior to pregnancy. As discussed, it may be difficult to establish aetiology of a single kidney and there is some overlap therefore in the populations.

A total of 11 women had a single functioning kidney following nephrectomy ($n=9$) or acquired atrophy ($n=2$): 2 women had Wilms' tumours in childhood, 2 sustained trauma, 1 woman was a living kidney donor, 2 women had scarred non-functioning kidneys removed secondary to complications of renal calculi or recurrent UTI, 2 women had atrophic kidneys thought secondary to recurrent UTIs and 2 women had a nephrectomy for unilateral multicystic kidney disease. For 15 women, there was a congenital cause for their single kidney. This was primary in 11 with 7 having combined URA and uterine anomalies, and 4 having isolated URA. Four had a secondary congenital cause, undergoing nephrectomy for congenital

Table 1. Demographics, booking characteristics and pregnancy outcome for women with an acquired single kidney.

Age	Ethnicity	Aetiology	Years with single kidney	Parity	BMI	Booking BP (mmHg)	Booking creatinine (μmol/l)	Complications	Gestation at delivery (weeks)	MOD	BW Centile
30	Black African	Nephrectomy – trauma	7	0	19	95/66	57	None	40	EMCS	5th
32	Black African	Nephrectomy – trauma	11	2	37	120/78	86	PET, PTB, UTI	35	SVD	25th
35	White other	Nephrectomy – hydronephrosis, calculi	7	0	22	130/80	81	PET	40	VD	50th
25	Pakistani	Nephrectomy – Wilms' tumour	22	1	19	102/60	73	UTI	39	SVD	25th
33	White British	Nephrectomy – recurrent pyelonephritis	21	1	26	100/68	83	Hydronephrosis, UTI	39	FD	50th
34	White British	Nephrectomy – Wilms' tumour	30	5	19	110/60	67	None	38	SVD	50th
37	White Irish	Nephrectomy – living donor	2	2	22	110/64	80	PN sepsis	41	SVD	50th
32	White British	Atrophic kidney	2	4	25	90/60	62	Gest.proteinuria, PTB, UTI	32	SVD	50th
17	White British	Nephrectomy – multicystic kidney	15	0	19	130/58	69	UTI	37	SVD	50th
31	Afro-Caribbean	Nephrectomy – multicystic kidney	4	1	28	120/70	77	PET	37	SVD	50th
20	White other	Atrophic kidney – awaiting nephrectomy	4	0	24	129/59	74	Gest.proteinuria	40	FD	50th

BMI: body mass index; BP: blood pressure; MOD: mode of delivery; BW: birth weight; UTI: urinary tract infection; PET: pre-eclampsia; PTB: pre-term birth; Gest: gestational; HTN: hypertension; SVD: spontaneous vaginal delivery; EMCS: emergency caesarean section; FD: forceps delivery; VD: ventouse delivery.

Table 2. Demographics, booking characteristics and pregnancy outcome for women with a congenital single kidney.

Age	Ethnicity	Aetiology	Years with single kidney	Parity	BMI	Booking BP (mmHg)	Booking creatinine (μmol/l)	Complications	Gestation at delivery (weeks)	MOD	BW centile
34	White British	URA	34	1	37	128/74	64	Gest. HTN, UTI	40	SVD	5th
35	Pakistani	URA	35	2	28	100/70	56	GDM	40	SVD	>99th
28	Asian British	URA	28	1	23	100/60	56	Pyelonephritis, UTI, FGR,	39	ELCS	<1st
33	Asian other	URA	33	0	23	120/70	63	UTI	40	FD	25th
26	White other	URA, absent fallopian tube	26	0	25	110/66	76	Miscarriage	–	–	–
38	White other	Nephrectomy – nonfunctioning pelvic kidney	29	2	24	111/62	77	Gest.proteinuria, UTI	37	SVD	50th
40	White British	URA, absent ovary and tube, unicornuate uterus	40	1	19	100/70	76	PET, UTI	36	SVD	5th
28	White British	Nephrectomy – bilateral vesicoureteric reflux, reimplantation of ureters	20	0	21	100/60	77	Hydronephrosis, UTI, puerperal sepsis	37	VD	10th
31	Arab	URA, uterine didelphys	31	0	24	127/55	59	None	37	ELCS	50th
31	Unknown	URA, uterine didelphys	31	0	19	112/62	53	Miscarriage	–	–	–
40	White British	URA, absent ovary and tube, unicornuate uterus	40	1	19	100/70	76	Lost to follow-up	–	–	–
36	White British	Congenital ureteric stenosis – nephrectomy	33	1	24	100/65	71	None	40	SVD	75th
28	Indian	Double ureter, partial removal with secondary renal atrophy	18	0	28	112/78	73	UTI	39	VD	25th
32	White other	URA, uterine didelphys	32	0	22	100/50	67	None	39	ELCS	50th
40	White British	URA, uterine didelphys	40	0	21	105/64	68	UTI	40	VD	25th

BMI: body mass index; BP: blood pressure; MOD: mode of delivery; BW: birth weight; URA: unilateral renal agenesis; UTI: urinary tract infection; GDM: gestational diabetes mellitus; FGR: fetal growth restriction; PET: pre-eclampsia; Gest: gestational; HTN: hypertension; SVD: spontaneous vaginal delivery; ELCS: elective caesarean section; FD: forceps delivery; VD: ventouse delivery.

obstruction, vesicoureteric reflux, atrophy following removal of a double ureter and removal of a non-functioning pelvic kidney.

They had been living with a single kidney for a median of 28 years (range 2–40 years), the shortest time being the only living kidney donor in the group; all but 5 of the others had been living with a single kidney for more than 10 years.

The women were from a variety of ethnic origins reflecting our local population in the greater London area. Their median age at booking was 32 years (range 17–40 years), median BMI of 23 kg/m^2 (range 19–37) and 2 were current cigarette smokers. None of the women had a medical history of diabetes mellitus, sickle cell disease, autoimmune disease or chronic hypertension. Only one had received any renal follow-up in adulthood. None of the women had received pre-pregnancy counselling in relation to their single kidney and none were aware of any risks associated with a single kidney; none were having monitoring of BP and proteinuria outside of pregnancy.

There was no clinical evidence at antenatal booking of pre-existing hypertension or proteinuria on dipstick urinalysis (except one woman who also had nitrite positive urine dipstick and a microbiologically proven bacteriuria). Baseline uPCR was tested in 13/26 with none having significant proteinuria (>30 mg/mmol). Levels ranged from 6 to 29.1 mg/mmol (median 13.0 mg/mmol). Since the study, we now have a consistent policy of testing urine for baseline uPCR in women with a single kidney, regardless of urinalysis result; however, this was not established beforehand and subject to clinician preference. There were no identifiable trends in baseline uPCR level and pregnancy outcome or renal function for this small group. Baseline serum renal function (urea and creatinine) was taken from the whole cohort. Booking serum creatinine concentrations ranged from 53 to 86 μmol/l. There are some differences in published reference ranges for serum creatinine in the first trimester of pregnancy, at the upper end, 50–82 μmol/l is suggested;[15] however, more recent publications use a lower range of 35–62 μmol/l.[16] While creatinine has limitations as a marker for renal function, it is concerning that 20/26 women in this series booked with a serum creatinine outside a conservative reference range for the first trimester or at the upper limit of normal.

A total of 14 women were parous (range para 1–5), of whom 12 had all of their previous pregnancies (totalling 21) while living with a single kidney. Four women (33%), of whom two had an associated uterine anomaly, had each had a single previous pre-term birth at 34–36 weeks' gestation. There was no history of extreme premature birth or second trimester miscarriage in the group.

The most frequent complication was UTI. For the purposes of this study, the term 'UTI' refers to both symptomatic infection with confirmed bacteriuria and asymptomatic bacteriuria; 13 women (50%) had at least one (range 1–3) UTI in the antenatal period including progression to pyelonephritis in a small group ($n = 3$). Of the 13 women who had renal function tested beyond a booking baseline, five had a rise in serum creatinine to greater than 90 μmol/l either in association with infection ($n = 3$) or hypertensive disease ($n = 2$). Nine pregnancies (35%) were complicated by pre-eclampsia (4), gestational hypertension (1) or gestational proteinuria (4).

The four women who developed pre-eclampsia ranged from 31 to 40 years in age with an average of 15.5 years of living with a single kidney, largely for acquired reasons (3/4). Despite three of the women having had at least one previous pregnancy to term, there was no

prior history of gestational hypertension or pre-eclampsia. Interestingly, the women had booking creatinine ranging from 76 to 86 μmol/l. All four women had vaginal deliveries from 35 to 40 weeks' gestation with babies weighing 2226–3690 g equating to 5th–50th percentile when encompassing infant gender. Three had severe late-onset pre-eclampsia occurring beyond 34 weeks' pregnancy with systolic BPs in excess of 160mmHg. In two of these cases, the women went into spontaneous, late pre-term labour at 35 and 36 weeks. One of the three women underwent labour induction for pre-eclampsia at 37 weeks and her case was complicated by posterior reversible encephalopathy syndrome. The fourth presented in spontaneous labour at 39 weeks' gestation with mild late-onset pre-eclampsia and moderately raised BP.

The majority of babies ($n = 19$) were delivered vaginally at 37 weeks' gestation or more, median birthweight 3233 g (range 2040–5124 g), birthweight percentiles ranging from <1st to >99th with a median of 50th percentile. There were three preterm births in the study cohort. One at 32 weeks' gestation in a woman with a nonfunctioning atrophic kidney who had had one of her four previous babies pre-term at 34 weeks. Two occurred spontaneously at 35 and 36 weeks' gestation in women who developed pre-eclampsia, both women had had a previous preterm birth: one had acquired nephrectomy through trauma, the other URA with associated unicornuate uterus.

No congenital renal abnormalities were identified in the neonates antenatally during routine anomaly scanning.

In general, all women received a plan of care, which included baseline blood tests for renal function in the first trimester, a plan to send urine for microscopy and sensitivities at each antenatal visit, prompt treatment of UTIs, retesting of urine on completion of treatment to confirm clearance and routine monitoring of BP and urine for proteinuria.

Conclusion

There is a paucity of published data regarding pregnancy outcomes in women with a single kidney from all causes. This consecutive cohort of unselected women with a single functioning kidney for longer than 25 years in the majority, have higher than expected serum creatinine, high incidence of UTI and high rates of hypertensive disease in pregnancy compared with the general pregnant population. Possibly of greatest importance was that none of the women were aware of the recommendation for lifelong follow-up and annual review of BP and urine for proteinuria. Overall, despite these factors pregnancy outcome whether the single kidney was acquired or congenital was generally favourable for mother and baby.

To address the limited knowledge of how to protect their single kidney and need for lifelong monitoring, we devised a Patient Information leaflet – 'Living with a single kidney, pregnancy and beyond' that highlights the importance of pro-actively caring for a single kidney lifelong, avoiding renal trauma and UTIs, being aware of common nephrotoxic medications, healthy diet and lifestyle and the importance of annual BP checks and urinalysis within primary care. This advice had not been given previously to any of the women in this cohort. We would be happy to share this leaflet with readers if contacted directly.

The women in this cohort had a high rate of UTI compared to an expected rate in pregnancy of around 20%.[17] This may be related to higher detection of asymptomatic bacteriuria from more frequent microbiological assessment of urine samples at each contact regardless of urinalysis result. This is important because we know that UTIs are responsible for a major part of all antenatal admissions and morbidity as well as being independently associated with adverse pregnancy outcomes such as pre-term birth and fetal growth restriction.[18] In women with a single functioning kidney, the consequences of an ascending UTI and impact on renal function may be greater and therefore early detection and treatment are essential. For this reason, we believe frequent testing remains an important management strategy in association with specifically educating women on how to reduce the likelihood of developing an infection and retesting urine after treatment is completed to ensure clearance.

We observed a high rate of hypertensive and proteinuric disorders of pregnancy, overall 35% with 15% suffering pre-eclampsia, compared to a background figure of 10% in the UK with a 3–5% risk of pre-eclampsia.[19] This correlates with Garg et al.'s[9] findings of gestational hypertension and pre-eclampsia in 11% of 131 pregnancies in a cohort of living kidney donors compared to 5% in a matched non-donor group of 788. It also supports the findings from a recent study of pregnancy outcome for women with URA in their first pregnancy in which the odd ratio for pre-eclampsia was 2.4 compared to a matched cohort.[10] Overall, these data suggest that women living with a single kidney are at greater risk of pre-eclampsia than previously believed. The negative impact of a hypertensive disorder suffered in pregnancy on future cardiovascular and renal health for all women is well understood. This may have graver consequences for women living with a single kidney although long-term outcome data for this particular group have not been published. We believe clinicians providing antenatal care for women with a single kidney should be more vigilant for hypertension and consider a target BP of <140/90 mmHg as advised by NICE for women with end organ damage from hypertension.[13] With evidence from post hoc analysis of CHIPS (Control of Hypertension In Pregnancy Study),[20] there may also be an argument towards lower BP thresholds of 130/85 mmHg although this needs wider consideration with evaluation in a larger dataset. At such levels of pre-eclampsia risk, we feel that low-dose aspirin prophylaxis is warranted. Women with a single kidney have largely been overlooked for prophylaxis in the past as most are not considered to have CKD and may not otherwise fit criteria.

There is some uncertainty about the long-term impact of living with a single kidney from childhood, our understanding being hampered by the biases and limitations inherent in long-term cohort studies exposed to changing diagnostic and treatment modalities. The median length of time that the 15 women with a congenital aetiology had lived with a single kidney was 32 years (range 18–40 years). This is concerning. Long-term studies of children with URA or nephrectomy in early childhood have demonstrated an increase in rate of proteinuria, hypertension and renal insufficiency that develops after 10–25 years,[11,21–23] including in some cases end-stage renal failure requiring dialysis.[24] Life-long follow-up with regular BP checks and assessment for development of proteinuria, in line with Kidney Research UK's position, is advised[11,12,25] and the culture of considering URA as a harmless malformation is discouraged.[11] This is particularly pertinent for this unselected group in whom the majority have congenital absence and have been living with a single kidney many years prior to pregnancy. They are at a potentially vulnerable stage in their kidney's function before the added stressors of pregnancy. This is partially demonstrable by 77% of the group already having a booking serum creatinine beyond the upper limit of normal first trimester creatinine. It is in contrast to living kidney donors, in whom much of our understanding of pregnancy outcome is based, who generally have donated in later years and lived with a single kidney for a short period of time prior to pregnancy.

Finally, it must be remembered that pregnancy and birth may expose the vulnerable single kidney to a number of other threats, for example hydronephrosis, hypovolaemia during obstetric haemorrhage, iatrogenic trauma to the renal tract during caesarean section or surgical management of haemorrhage and routine use of non-steroidal anti-inflammatory drugs for post-partum pain relief. These rarely have a significant impact on the pregnancy but may

have long-term consequences for the woman's health and future function of her solitary kidney.

Following on from this study and its findings, we have developed a consistent policy of care within our department for pregnant women known to be living with a single kidney. This includes an initial assessment within the Obstetric Medicine service, baseline serum creatinine and urea, uPCR, BP and mid-stream urine for culture and sensitivities, initiation of low-dose aspirin for pre-eclampsia prophylaxis and provision of our leaflet. A renal ultrasound may also be required, depending on the aetiology, baseline investigation results and the time period since the last renal scan. This is followed on with a plan to send urine for culture at each contact with a health professional and low thresholds for pharmaceutical BP management as discussed.

Women living with a single kidney should also be offered preconceptual care. This and the above strategy of antenatal care offer a unique opportunity to encourage women to life-long renal protection, lifestyle modifications, measures to avoid renal tract infections and ongoing screening for hypertension and proteinuria. This is another situation where antenatal input can offer long-term benefit to the woman over and above the short-term goals of the pregnancy.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article..

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval was not required as this was an audit of practice.

Guarantor

SS.

Contributorship

SS completed data acquisition, analysis, literature review and wrote the first draft. JT contributed to initial concept, design and data acquisition. LP and JG contributed to the concept and revision. All authors reviewed and agreed to the final version of the manuscript.

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